

MANAGEMENT OF PACHYDERMOPERIOSTOSIS WITH BISPHOSPHONATES, ISOTRETINOIN AND COLCHICINE – A CASE REPORT

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ABSTRACT

Pachydermoperiostosis is characterised by pachyderma (Cutis verticisgyrata or thickening of facial skin or scalp), periostosis (hypertrophic osteoarthropathy or thickening of bones) and digital clubbing. We report an interesting case of 27-year old male who came to the hospital with coarseness of face since two years, bumps over scalp, and widening of nose, hands, knees, feet, fingers and toes with Grade IV clubbing of fingernails, excessive folds over the scalp with increased furrowing of forehead. Skin thickening seen over nose, cheeks & chin. Radiological examination showed broadening of bones of knees, hands and feet with no restricted mobility. After evaluation and confirmation of diagnosis, and reviewing the literature, the treatment has been started. Seborrhea was managed by Isotretinoin for three months and bone pains, which developed two months after diagnosis with bisphosphonates. Colchicine was added to the treatment. The patient tolerated the drugs well and coarse features and bone pains subsided. Starting the bisphosphonates in the early stages has a beneficial role in the management.

KEY WORDS

Pachydermoperiostosis, osteoarthropathy, Bisphosphonates, Isotretinoin, Colchicine.

INTRODUCTION

We report an interesting case of 27 yr old male who attended the hospital with complaints of coarseness of face since two years, bumps over scalp, and widened parts of fingers.

Patient was asymptomatic two years ago, coarseness of face developed gradually associated with excessive folds of the skin of the forehead and scalp. This is not associated with any discomfort. Gradual broadening and thickening of the hands, knees, feet, fingers and toes was noticed. History of cool extremities and excessive sweating was present. There was no history of neurological deficits.

CASE REPORT

Patient was moderately built and moderately nourished, with Broadening of nose, hands, knees, feet, fingers and toes (Fig 1), with Grade IV clubbing of fingernails (Fig 2). Cutaneous examination revealed excessive folds over scalp (Fig 3), with increased furrowing of forehead, skin thickening seen over nose, cheeks & chin (Fig 5). On palpation skin is coarse in affected areas. Hair nails & mucosae were normal. Skeletal Examination revealed broadening of bones of knees, hands, and feet including fingers & toes with no restricted mobility. On palpation, thickening is felt in the bones of forearms & legs. All other systems were normal.

Based on these findings, conditions such as Pachydermoperiostitis, thyroid acropachy and

Acromegaly were considered in the differential diagnosis.

Routine investigations revealed that CBP, CUE, BSL – Fasting & Post-prandial, Renal parameters, LFT, Lipid profile were all within normal levels. ESR was raised to 120 mm/hr and Sr. Calcium was found elevated, Glucose tolerance test, Thyroid profile, Prolactin assay, Growth hormone assay were normal. Skin biopsy had revealed sebaceous hyperplasia and dermal edema (Fig 6). X-ray skull, hands and feet (Figs. 7, 8, 9) revealed thickening of skull bones. USG abdomen – NAD. Imaging including MRI and CT scan of the Brain – no evidence of pituitary adenoma. Fields of Vision: Normal. Radio-isotope bone scan (Figs. 10, 11) shows evidence of thickened bones & periosteal reaction. Gastroendoscopy revealed normal gastric cavity.

Two years ago patient was apparently asymptomatic (Fig 1.). He was diagnosed as a case of Pachydermoperiostosis based on the features of cutis verticis gyrata (pachydermia), broadening of bones (periostosis), clubbing, normal levels of hormones (which will be elevated in thyroid acropachy and Acromegaly). Patient had a family history wherein his distant (3rd) relative was diagnosed as having the same condition. After the Diagnosis was made, in view of seborrhea, patient was started on Isotretinoin 40 mg /day and on colchicine for the thickening of sub-cutaneous tissues, reviewing the literature. After 3 months of therapy, Isotretinoin was tapered and stopped, when patient had improvement in sebaceous hyperplasia.



Fig 1: Periostosis of knee joints with bony enlargement



Fig 2. Clubbing of grade IV of all the finger nails.

Patient has developed bone pains after two months of diagnosis, which were initially not present. He was started on bisphosphonates. Meanwhile, treatment with colchicine is continued, bone pains improved 3 weeks after bisphosphonates and coarse features lightened on continuous treatment with colchicine. Patient tolerated the drugs well. Self limiting nature of the Disease was explained to the patient and he was re-assured. The efficacy of bisphosphonates has been very good along with good tolerance by the patient. Isotretinoin improved his seborrhea. Starting of Bisphosphonates in the early stages has a beneficial role for the management of these rare cases. Though, BTX- A has been tried in three patients as reported earlier¹⁰, as the patient couldn't afford botox we had a cheaper option of Isotretinoin.



Fig 3: Cutis Verticis Gyrata.



Fig 4: Normal appearance at the age of twenty.



Fig 5: Present photograph of the patient.

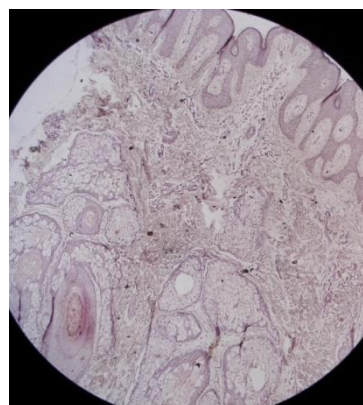


Fig 6: H & E stain showing increase in no. of sebaceous glands.



Fig 7,8,9, X-ray of hands, knees and feet showing perisostosis.



Fig. 10 & 11. Skeletal scintigraphy showing evidence of cortical thickening of long bones.

DISCUSSION

Pachydermoperiostosis is characterised by pachyderma (cutis verticisgyrata or thickening of facial skin or scalp), periostosis (hypertrophic osteoarthropathy or thickening of bones) and digital clubbing. It is a primary form of hypertrophic osteoarthropathy, wherein the secondary form involves the pulmonary or cardiac or neurological systems¹. It was first described by Solente and Gole in 1935, hence also known as Touraine-Solente-Gole syndrome². There are three forms, complete form with all three features of pachydermia, periostosis and digital clubbing, incomplete form-without skin involvement and forme fruste-clubbing and pachydermia are present with no bony involvement³.

The diagnosis of PDP is based on the presence of at least two of the four criteria set by Borochowitz which are a (1) history of familial transmission; (2) pachyderma; (3) digital clubbing; and (4) skeletal manifestations, such as pain or signs of radiographic periostitis⁴. Though there is abnormal peripheral microvascular blood flow there is a role of endothelial hyperplasia and connective tissue showing hyalinosis and sclerosis, also sebaceous and eccrine gland hyperplasia was noted⁵.

Histopathologic examination reveals an increase in dermal collagen with variable degrees of overlying hyperkeratosis and acanthosis⁶. Mucin stains of skin biopsy specimens may reveal

increased dermal mucin deposits⁷. Electron microscopy has shown that the collagen fibers from the involved sites are smaller in diameter and less uniform than normal collagen fibres⁸.

Seborrhea is noted in more than 90% of cases, with, sometimes, occurrence of acne lesions or folliculitis. Hyperhidrosis is also frequent (44%) particularly in the hands and the feet and sometimes in the major folds. Pubic and facial involvement is always rare⁹.

The therapeutic options, mainly symptomatic, were mainly directed towards bone pains, swelling or effusions.

For pachydermia patients, their main complaints are due to gross appearance, oiliness and hyperhidrosis. The main reason for the coarseness is due to the mucin deposition with excessive seborrhea. This can be managed by Isotretinoin in a dosage of 1 mg/kg/day (upto a cumulative dosage of 8 grams). For hyperhidrosis, 6.75 % -20 % Aluminum Hexa Chlorohydrate can be tried. Though oral agents such as propantheline bromide (15 mg TID) are beneficial they may have troublesome side effects. There have been reports of BTX-A has been tried in three patients with appreciable results except in one patient wherein there was an exacerbation of lid ptosis¹⁰. Plastic surgery may improve the appearance of the face and scalp by excising redundant skin and correcting the cutis verticisgyrata. Bilateral blepharoplasties, tarsal wedge resections, excision of skin furrows, and

facial rhytidectomy have been described as methods of providing cosmetic improvement^{11, 12, 13}. In late cases, wherein leonine facies is formed, surgical excision for good cosmetic results is a very good option.

For bony pains – NSAID's, Indomethacin, colchicine can be given for symptomatic relief¹⁴. Bisphosphonates especially risedronate of dosage 35 mg orally once a week taken with adequate supplementation of Vit D and calcium, or pamidronic acid or olendronate can be given. Bisphosphonates inhibit osteoclastic bone resorption and therefore reduce bone remodeling and alleviate painful polyarthriti¹. Infliximab has been tried but has been less effective¹⁵.

CONCLUSIONS

In our case, patient had complete form of pachydermoperiostosis, along with radiological features and histological features. The patient responded well to Isotretinoin and bisphosphonates had relieved the patient from bone pains. Isotretinoin should always be considered as it is sebostatic and also has role on control of fibroblasts.

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